Suppl. 10 with its Supplements too.

Mister John G Roberts Jr, Chief of Supreme Court,

1 1st Street, NE, Washington DC, 20543-0002, USA. Paris, 11th July 2006.

From Dr.Y.Zagyansky, Entraide, 22 rue Ste Marthe, 75010 Paris France

Dear John G Roberts, Chief of Supreme Court of United States ! I must write at level of such famous High Court because of the most Terrible nightmare of Crimes of XXI century at highest all coordinating ExtraGovernmental United States level!

Accusation in Crime Against Humanity. I accuse the most powerful HyperTotalitarian Organization of USA and logically "much much more", ruling de facto The Governmental US Patent and Trademark Office (USPTO) in sure simple intentional atrocious Crime against Humanity and against People of United States: cold assassinations of millions of victims of AIDS with sure projection for continuation of such assassinations because of only one Revolutionary (see his numerous antifascist ISBNs). The proofs are archinett and simple.

By outstanding primitive demagoguery of Time of Tribunals of Inquisition and Powerful Hunters of Witches (always alive but adapted and re-coloured to Nights of Humanity and their Good Days), without any obligatory concrete discussion and correction, Governmental USPTO criminally usurped the Elementary Rights of Humanity even to discuss and usurped Law (surely including International one of International Application), rejecting (criminally, openly according to Penal Code) the Application of XXII century with sole means against Pandemic of AIDS and Mad Cow, conducting to cynical Crime against Humanity (possible as unpunished again at their Good Days). By chance for this revolutionary Author (for millions of victims of AIDS and for People of World to realize the Time of Reigning Illegality for the Honests), the USPTO really gave however one sole example (the basis of all rejections!), but which.... reveals elementary unlegal unskilled USPTO Examiners. USPTO Examiners surely stipulated that macrophages do not leave the blood vessels. However elementary for each nowdays student, they ***DO*** traverse them for site of infection in tissues. But already this elementary means that USPTO Examiner do not know at all whole field of Molecular and Cellular Biology and Immunology, means of all proofs of Invention, that surely signifies that, without doubt, such unqualified "Examiners" could not read the text and made their Demagogy to reject without any sense, any real knowledge, but criminally, like by prepared in advance text for anything! Specially! Penally! Consequently, in connection with millions of intentional victims of AIDS, this is already sufficient for highest punishment of logical Murderers and Assassins = Criminals against Humanity!

Secondly, I accuse United States Government for ArchiBrigandage (many milliards) at intentional stealing (because of certain political convictions of antifascist author) and utilizing

simple clear means against Mad Cow (BSE) of the same published Application (since 2002-2003), avoiding, by rejecting the Patent, to pay milliards as fines for stealing in spite of Crime against Humanity.

You can see all details for exemplary condemnation for open Crime against Humanity in Supplements, wherein in complete openness, I transmit you also my answer to Governmental Responsible of USPTO. Sincerely yours Dr.Y.Zagyansky

SUPPLEMENTS:

§1. Concrete details of certain unqualification of USPTO Examiner who surely could not even read Application because of unqualified level.

At elementary idiotic grotesque, appointed (logically by Criminal Ruling Organization in USPTO) Primary Examiner (Mr. Jeffrey Stucker) not only did not read the essential of Patent Application [N°US 10/505,353- National phase of International PCT/EP02/02302 (see yet complete file in USPTO Register by http:/pair-direct.uspto.gov): "End of AIDS for General Virology, based on profound science as protein foldings: safe vaccines, universal antimicrobial means, mad cow end"], but he a priori surely could not read it with professional understanding because manifestly he is not skilled person and, without doubt, he knew all this perfectly, that is too grave and surely criminal with his such too arbitrary "conclusions".

So de facto, in knowing own absence of any serious possibility for reading and understanding, it is intentional crime to write: all "claims 1-12 (it means all invention) are rejected.. as containing subject matter which are not described in the specification" (it means text) (claims are asked protections: for my new products or processes). And such unlegal global Declarations without concrete discussion but from one of the most prestigious Authority of Governmental US Patent Office had to destroy any answer, any resistance of Revolutionary, because de facto, "normally" this had to be supreme order to all employees of USPTO without any discussion and corrections again. [About such experts and "experts" of American Offices, see book of (measured? and coordinated? In logical Desert de facto) Known American resistants John Stauber and S.Rampton: "Trust us, We're Experts! How Industry manipulates Science and gambles with your future"].

And only due to superchance, "Their Majesties" gave however one "entire"! example (as OverLord's chance for even provability of real arrogant Enemies against Humanity without borders in real camouflaged Desert) and.. it is already more than sufficient certainly to accuse them: it was demonstratively manifestly unskilled man and all written by such man must be also purest intentional falsifications with open 100% Crime against Humanity. "Examiners" wrote: "An example of some unclear, inexact or verbose terms used in the specification are

Yu Zag for USPTO

(sole "example" and with "are"?? They want to jump as Baron Münch.. or rather from Münch..?): "It is proved that it is only the moving macrophages that are contaminated during movement". It is not clear what is meant by: "only the moving macrophages" because macrophages are in the circulating blood and are always moving".

De facto it is exemplary nonsense. In taking from Fundamental Internet "Web of Science" with ALL best World professional literature for many years only articles (always professional, specialized), which only sole contain even titles with the same (so called "unclear, inexact or verbose terms"): "moving or migrating macrophages or lymphocytes or monocytes", one shall see 10 professional articles of specialists (all with YZ sense) as "Localization of.. proteins in **moving macrophages**" from Stanford University in Mol.Biol.Cell 7, 2204 (1996). It is already de facto 100% nonsense of USPTO unskilled 1st "Examiner". In taking any presence in Abstract of words: "(macrophage or lymphocyte or monocyte) and (moving and migrating)", one has 944 results!, wherein I saw only the same YZ result! It is already **de facto** 100%!

But it goes much farer. The macrophages in noncirculating (of course) tissue are not always moving, evidently. So words of "Examiner": "macrophages... are always moving" are complete nonsense, because "Examiner" simply does not know the too elementary: macrophages (leukocytes) can move into tissue from bloodstream.

It clearly proves that such "Examiner" does not know at all Molecular and Cellular Biology and Immunology wherein "The migration of white blood cells out of bloodstream (justly this case) into sites of infection" (text even from Fig.24-15) is known from elementary Manual N°1 for students [Alberts B (President of US Acad. Sci) et al "Molecular Biology of Cell"] (or also classical student Manual "Cellular and Molecular Immunology" Abbas AK, p.255). But even nowadays **students** in Molecular and Cellular Biology and Immunology, all, know that macrophages traverse the walls of blood vessels for sites of infection. It is incredible revelation of absolute noncompetence of unskilled old fashion Examiner, level of which could choose and find only such **sole** obstacle of **real** de facto "understudent"unqualification to cancel by demagogy and unlimited special unpunished power even grandiose series of discoveries of XXII century without any concrete discussion. **ANYWAY IT IS ALREADY DONE FOREVER: Examiners without sure possibility of reading with understanding the text (due to sure proven already noncompetence) made Crime against Humanity a priori!**

Moreover, all proofs of 101 pages of my very fundamental work with about 900! References (with the same terms!) for experimental works (Precedent Art) were done with

means of such Molecular and Cellular Biology and Immunology that "Examiner" did not know at all and he must be like clinician of Medicine with surely very old scientific medical bases of 40 years old. It is not "error" of Examiner! It is not to know real: 2 x 2 = 4 and to pretend to teach "Differential Equations" with Crime against Humanity, knowing that "Examiner" even cannot read them!

§2. But "Remarkable" according to even Great Scientists.

This sure crime against Humanity is underlined by leading Scientists. 1st small part of this work (with the same English terms) was not only understandably written but it was estimated as extraordinary by Georges Mathé, President of French Specialized Institute of Cancerology and Immunology (Gold Medal of Academy of Medicine of 2004), Honorary Main Editor of International Journal, author of numerous International Editorials: "With success for your remarkable composition!". And certainly world level specialist of AIDS, chief of laboratory in best Paris University Prof. Zagury even wrote: "Unfortunately I am not qualified to evaluate with utility your work and moreover less to criticize it" (with similar letter of President of National French AIDS Council later). And President of French Acad. Sci. (justly World specialist in Immunology) Jean Hamburger recommended me in Acad.Sci even for immunological Introduction (with English terms) to this work (text published in Publ. FR2711318, p.1).

So it is fantastical: best World specialists of AIDS consider, in 10 Years, the work of author (who is also author of professional publications in "Science", "Nature", "Immunochemistry" etc from best World Institutions where he worked as Inst. Molecular Biology Acad. Sci. USSR with PhD in field, Johns Hopkins University, College de France, Institut Pasteur) much more developed than their own level even for small part of this GRANDIOSE work but unskilled man, who certainly knows too much less than leading Prof.Zagury, reject titanic work, that he certainly (see above) could not even read. And it is with sole possible solution of Epidemic of AIDS, that this logically Ordering Criminal Totalitarianism must also know. But it is blaspheme of any existence of Civilization, it is Hymn to victorious Enemies of Humanity and I accuse this Totalitarianism and its Executor who must be (all) exemplarily punished! (See details in Supplement as justly finished works: as "To stop tragedy Human at Horror of well underestimated Pandemic: all searched means against AIDS are scientific nonsense, except sole basic ignored solution")....

§3. All it certainly looks as Strategy of one World Totalitarian Organization to cut Revolutionary by any way!

Yu Mau for USPTO

This is National US phase of International Application wherein Determining Examination (Search) was done already by International Search Authority (ISA) (European Patent Office-EPO in this case) that governs (see: obliges) the global work of Examiners at National Phases. EPO makes the same Examination at International phase for USPTO too.

So globally, USPTO National Examiner is obliged to do nothing serious [moreover, the same Examination, EPO (ISA) had to make for USPTO too!]. Moreover, EPO and USPTO signed "Memorandum of Understanding" about "harmonization or standardization of Search strategies and substantive Patent Law". And justly EPO (ISA) terribly made this Examination with proven falsifications wherein globally EPO did not examine a number of claims because they are "scientific theories" (it means: precise, solid) and did not examine therapeutic processes (with patentable products). These formal unlegal (see: even criminal) things were easily and clearly destroyed by me, especially in last answer (10/22-27/2005) (see EPO Register: www.epo.org, later Epoline and Register). But even in spite of intentional falsifications! and intentional attempts (complete fiasco after my answers) to destroy Patent, EPO wrote nothing that now USPTO "Examiner" proclaimed **NEWLY**. It again confirms impertinent arbitrary of Totalitarian System wherein moreover "scientific theory" means precise, solid confirming again intentional crime of Demagogy of empty words.

EPO has the problems to answer: too open Crime against Humanity can be very heavy! So as the same Totalitarian Criminal Organization, USPTO does not take these destroyed (but not answered during 8 months by EPO) precise arguments that USPTO must follow… In such situation, for obvious effectivity, I sent Fax (11/28/2005) (receipt N°FA1-03-55953) in asking to suspend action for 6 months to wait ISA (EPO) determining International answer. But, very strangely, there is no such Fax in file??? (in spite of parallel e-mail) wherein another Fax (N°FA1-03-55964) from the same post and time is in the file of my other application (10/508,967). So with this intentional (as I think) disappearance, USPTO Organization justly began new type of Campf: unconcrete Demagogy which is undiscussible. Only by chance of sole example, revealing surely complete absence of corresponding level to read, I proved intentional Crime against Humanity! EPO obligatory answer must confirm it, especially after accusation in Brigandage with stealing and using the means against terrible Mad Cow by European Governments, that European Court justly shall see.

§4. Appointment of "Examiner" Jeffrey Stucker: is he one of special pertinent agents of Criminal Totalitarianism, really Ruling Organization in USA and the Rest?

But how expressively uncompetent unskilled Examiner received this file? File was received by Technology Center 1600 and its Department 1640: "Immunology, receptors/ligands…

Molecular Biology" and directed to this Art Unit 1648. And how Chief of this Unity Mr.Bruce Campbell transmitted it to unskilled (but special!) man? Is this special man who wrote terrible Demagogy of Crime against Humanity and who can take what he want after his received criminal task? What interests he had "to examine" such work, wherein his level does not permit even to read text! It is important problem: who really gives order in USA: agents? And Supreme Court?

Such strange appointment and Totalitarianism were demonstrated even in my 1st USPTO Application (1988). Examiner Jeff Kushan made complete exemplary Search (although I was complete Novice before tens and tens Applications). He sent me two Patents as simple matrices to correct form of already very positive searched claims, that I very simply did. But suddenly such my answer arrive not already to J.Kushan but to another person (Marg. Moskowitz), who denied already recommended and done! And no letter from already positive Examiner Kushan. Later I received "Notice of abandonment" that I did not answer for letter of 12-19-88 that I never received (logically from Mr.Kushan). Any my letters to USPTO to have this "abandoned" not received letter were without any (any!) answer. It was loss of millions of litres of human blood with.. similar principle as working Mad Cow! Is it not Open Brigandage of Governmental Office ("Democracy in Action") against Revolutionary even at already done principally Patent? The same appointment of special man, ready to do everything for Totalitarian Organization?

It means from beginning USPTO made the exemplary Examination even for complete Novice of my 1st Application of 1988. But when I made English terms Application (PCT/IB00/00843) in new for me field of global Theoretical Physics (wherein I do not have PhD, experience in best World Schools, 30 publications in best International journals), moreover with proven End of Einstein-Bohr Physics, the Dutch (Foreigner) Examiner Mr.Capostango understood all and made complete positive even exemplary Search (with all serving terms in New discussible science). It is, otherwise de facto complete intentional political demagoguery of English speaking Totalitarian Organization without Law! It is too obvious nonsense! To stop it!

§5. Totalitarian Criminal Network of all World Science logically participate in atrocities of Crime against Humanity because of only one Revolutionary!

But is it impossible, it is too much, Dr.Zagyansky! Of course too much! And to prove such criminal Infernal Machine against Humanity (with fantastical Theatre of Solid-like Magicians-Actors: "Trust us, we're Experts") is really impossible except the same chances!

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Cancer! Antiretroviral Therapy HAART (Highly Active, moreover) can stop division of cancerous cells and Medicine utilizes HAART to stop cancers at AIDS. But they all do not use it at all against all other cancers with this evident idea, moreover published very knowingly. So logically Big K° knows that HAART is too dangerous and they can "fantastically" arrange that nobody uses it.

So they claim everywhere the success of highly active HAART (see Fig. 4 from Fauci AS et al Emerg Infect Dis 11, 519, 2005 and Fig. 1b from Weiss RA Nat Med 9, 887, 2003), logically only to make appearance that situation is not so tragic. And consequently sole means against AIDS can be however stopped without special danger (as openly by USPTO). Moreover, in written detailed article: "HAART must signify Highly active ART to kill and has to be stopped urgently: Evident proofs" (for submission), I confirmed such prudent fear of logically knowing Criminal Totalitarianism!

There is Special overpowerful Network that makes plans and executes political persecutions of honest Resistants-antifascists. It is impossible to prove it as nett. But there is clear sure case. Already after two years after University, I made world discovery (confirmed) and was cited by very famous scientist (C.Tanford) in best mondial Review (Dorrington and Tanford, Adv Immunol 12, 333, 1970) for about one page!! But in famous "Science Citation Index" ("Web of Science"), one will not find such important citation of our article (Zagyansky et al Immunochemistry 6, 787, 1969). It is sure de facto Mondial political Spider Web: K° eliminated, from Internet, the citations of justly articles of Advances in Immunology (best reviews, only several for year! It is impossible) around 1970 but they had to leave more ancient citations from this journal with Nobel Winners!... It confirms real Industry of political persecutions in Science.. and in Patent Offices, evidently, surely, criminally, even with sure falsifications at intergovernmental level!

§6. Preliminary Accusation of United States Government in intentional stealing and robbery of preparation against Mad Cow [Appl. US 10/505,353 (PCT/EP02/02302)] with covering it by certain intentional falsifications to cut said Patent.

After book of 1997, "Mad Cow USA" written by known official Resistants in USA (measured?), characterized as "[the authors] have done the legwork and research necessary to produce a solid accounting of the affliction of mad cow disease" ("Chemical & Engineering News, 04/20/1998), the real announcement of disease by US Government (12/23/2003) reveals the presence of very probable even Epizootic in USA, especially in situation wherein even known means of spreading were not forbidden in USA. Only defence of meat and bone meal (made from killed cattle and used to feed the new animals) in France costs 6 milliards of

Euros ("Impact Medecine" N°166, 06/22/2006, see here) (it means about 80 milliards of $ in USA).

.... The situation at 2002 was tragic in Europe (data more accessible according to above book too). "The number of cases continues to increase in the UK" [Review, Ghani AC Microb Infect 5, 385, 2002]. "In 2003 (work was made in 2002) in an updated study Fergelson and Donnelly... estimated that 4000000 (which even scale!!!) British cattle has been infected by BSE" [Supervie V C.R.Biologies 329, 106, 2006]. And vigilance was extraordinary: "It is unadmissible that 10 years after their ban, the traces (EVEN!) of meat and bone meal can be found in feeding of bovines... I do not ignore economical and technical problems... However the case of elimination of meat and bone meal and of systematic screening must be fixed..." French President Chirac (10/25/2000). However this crisis costs 90 milliards of euros to Europe... Pessimism reigned for many many years....

And suddenly the Miracle! In March of 2006, embargo for British meat is removed! In May of 2006, there is re-introduction of fish meal (contaminated usually with cattle meal) must be done. (That was justly recently banned as "serious problem which may prolong the BSE epidemic" according to European Scientific Committee). "European Government ("Commission") programmes the return of meat and bone meal in 2 years" ("Impact Medecine", N°166, 2006), that was justly demonstrated as the most dangerous in Epizootic [Baron T Pathol Biol 53, 229, 2005]. Fantastical!.Now ALL, with animals, are becoming Crazy!...

But how does it happen? With Dr.M.Eliaszewicz (Chief of French special State central Commission for Control), everyone see only the same used means as defence of suspected animal meals and systematic screening. But justly at the end of 2002, my this great Application was published. To synthesize miraculous peptides (small protein "Du-2T" of prion of appr. 20 amino acids) is routine and invisible as we see here de facto too (**in reality logically by the same PROVEN falsifiers of Governmental Offices**!!). Let's see. Before: "when a case of BSE is identified , the entire herd is usually slaughtered". And NOW: "animals which appear to be healthy could be used until end of their lives" ("Environment" 04/25/2006)! And why else, except such simple Miracle! Of course, surely, only if easily to inject such peptide [YZ US 10/505,353 (PCT/EP02/02302)]... So logically, only in such already solved and "used" situation, US Government admitted justly, at the end of 2003, "one" case of Mad Cow in USA. And of course, as in Europe: now the embargo for US meet is removed in Japan and other countries! All is o'key... We can see other proofs. All proven international falsifications by European Patent Office were done without any border between

for USPTO

Nationalities of EPO employees, as one Spinder's Overgovernmental Organization of course with Great known USA Totalitarian dominating SuperOrganization, as we see in common systematic Brigandage of Superpatents of Revolutionary Antifascist (see his ISBNs de facto) even with accusation in Crimes against Humanity. (They simply play game with resistants-dissidents as "cat with mouse": which "democracy" with "Posts" and "Times"!).

But there are strange cases. According to European Statistics (that of course, in such situation, could be more "imaginative"), a number of cases of Mad Cow (BSE) sharply decreases in UK and France, but oppositely it increases in New East European members (Poland, Czech Rep.). Of course, Old (see my Historical books) Totalitarian Criminal Organization does not believe yet (it needs more [known to them] spread corruption etc for complete slaving) to new members in Common Crimes as Governmental! Steeling! "The European Government discusses about removing of means for precaution without asking opinion of Authority of Food Security" (ELSA)", Dr. Eliaszewitz worries ("Impact Medecine" ibid). And Why? Justly there are de facto East European members in such Authority and they (ancient Socialist countries!!!) yet do not participate in Common Crimes: to avoid!

Sure action of preparations will be surely confirmed experimentally = stealing for 99.999% and "The Supreme Court" would be as Guardian of Brigands and Assassins of Jungles of Witches.

So I transmit to Supreme Court of USA Accusation to stop Crime against Humanity of US Governmental Patent Office (USPTO) and preliminary accusation about US Government steeling of means against Mad Cow. Sincerely yours Dr.Y.Zagyansky

Supplements: 1. Answer to USPTO of 07/10/2005 with all its Supplements. 2. Copy of **Exemplary Complete Search** made **yet in 1988** by USPTO even for my much less formally developed 1st Patent Application. 3. "Notice of Abandonment" (09/18/89) due to letter of USPTO of 12/19/88 (as unanswered), that I never received (and could not receive in spite my numerous letters to USPTO without any answer). 4. Fig. 4 of Fauci et al Emerg Infect Dis 11, 519, 2005 and Weiss RA Nat Med 9, 887, 2003 5. Copies from "Web of Science": a) Citing of article: Zagyansky et al Immunochemistry 6, 787, 1969 at page where the citation by Dorington and Tanford Advances in Immunology 12, 333, 1970 had to take place (but missed); b) Source Index: page with articles of "Advances in Immunology" with jump, logically too specially, from 1976 to 1964 (justly without 1970) that led to absence of JUSTLY exemplary citation by grand Tanford (and Dorrington). 6. Long text of grand citation (by famous Prof. Tanford) of Zagyansky et al 1969 (grand independent discovery,

already 2 years after University). 7. Confidentially, the text of justly written article: "To stop Tragedy Human of Horror of well underestimated Pandemic: all searched means against AIDS are scientific nonsense, except sole basic ignored solution" (without 2 lines of p.2) that will be sent together with articles: "Antiretroviral Therapy- "HAART" must signify Highly Active ART to kill and has to be stopped urgently: evident proofs" and necessary basic: "Errors of heart of Immunology: completely erroneous general structure of main receptors and Principal Scheme of Immunology" that will be sent to Prof.Mathé's journal (by himself as Founding Editor of his International Journal in such too special case). 8. "Impact Medecine" N°166, 06/22/2006, pp.6, 8.

Y. Zagyansky to USPTO

Suppl. 2 (To Cont'l)

exp. USPTO

FORM PTO-892 (REV. 3-78) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	SERIAL NO.	GROUP ART UNIT	ATTACHMENT TO PAPER NUMBER	
NOTICE OF REFERENCES CITED	096539	183		3
	APPLICANT(S) Zagyansky			

U.S. PATENT DOCUMENTS

*		DOCUMENT NO.	DATE	NAME	CLASS	SUB-CLASS	FILING DATE IF APPROPRIATE
	A	4,661,586	4/28/87	Levy et al	530	388	11/17/87
	B	4,690,893	9/1/87	Mosmann	530	387	5/13/85
	C						
	D						
	E						
	F						
	G						
	H						
	I						
	J						
	K						

FOREIGN PATENT DOCUMENTS

*		DOCUMENT NO.	DATE	COUNTRY	NAME	CLASS	CLASS	SHTS. DWG	PP. SPEC.
	L								
	M								
	N								
	O								
	P								
	Q								

OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)

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EXAMINER	DATE
Kushan	7/12/88

* A copy of this reference is not being furnished with this office action.
(See Manual of Patent Examining Procedure, section 707.05 (a).)

Suppl. 3 (To Cont.)

UNITED STATES DEPARTMENT OF COMMERCE emp. USPTO
Patent and Trademark Office

Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	RECEIPT DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
07 175,487	11 22 88	ZAGYANSKI	

Y. ZAGYANSKI
28 RUE DE TOLBIAC
75013
PARIS, FRANCE

DATE MAILED: 04/18/89

NOTICE OF ABANDONMENT UNDER 37 CFR 1.53

Regarding the Notice to File Missing Parts, dated 12-19-88, no response was received.

Therefore, the above identified application is ABANDONED.

Note: When an application is abandoned for failure to pay the filing fee, the application will not be retained (i.e., the application papers will be disposed of) copies of the application will not be provided or certified, and benefits under 35 USC 120 and 37 CFR 1.78 will not be accorded unless the processing and retention fee set forth in 37 CFR 1.21(l) is paid within the one year period set forth in 37 CFR 1.53(d).

A petition to the Commissioner under 37 CFR 1.137(a) may be filed requesting the application to be revived.

Under 37 CFR 1.137(a), a petition requesting the application be revived on the grounds of unavoidable delay must be filed promptly after applicant becomes aware of the abandonment and such petition must be accompanied (1) by an adequate showing, verified under oath or declaration, of the cause of unavoidable delay, (2) by the required response to the above identified Office letter, and (3) by the petition fee set forth in 37 CFR 1.17(l).

37 CFR 1.137(b), (unintentional delay) does not apply to revival of applications abandoned under 37 CFR 1.53(d) for failure to complete an application.

Any questions concerning petitions to revive should be directed to Petitions Information. (703) 557-4282.

Marsha D. Gentry/NB
Special Processing Branch
ONIAR, Application Processing Division
(703) 557-3831

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EMERGING INFECTIOUS DISEASES

Volume 11, Number 4, April 2005

Emerging Infectious Diseases: a 10-Year Perspective from the National Institute of Allergy and Infectious Diseases

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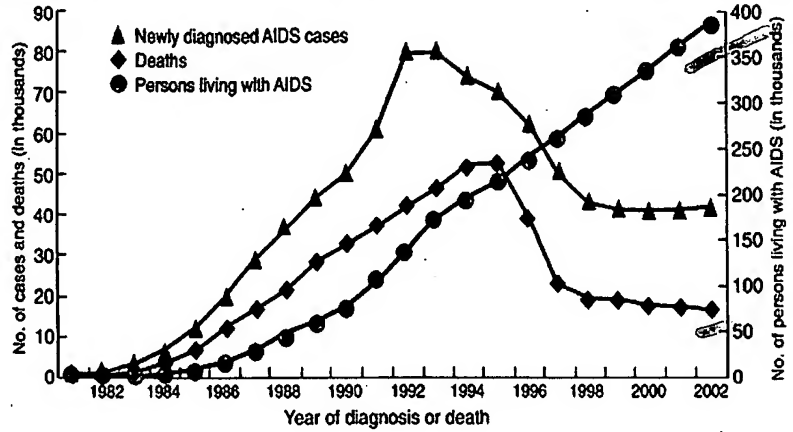

Back to article

Figure 4. AIDS cases, AIDS deaths, and persons living with AIDS in the United States, 1981–2003. Over the past decade, the number of new AIDS cases and deaths due to AIDS has decreased, while the number of people living with the disease has increased, due in large part to improvements in diagnosis and treatment. Estimates adjusted for reporting delays. Source: CDC (8).

This page last reviewed March 14, 2005

Emerging Infectious Diseases Journal
National Center for Infectious Diseases
Centers for Disease Control and Prevention

Suppl. 4 (To Cmte)

COMMENTARY

R.A. Weiss, HIV and AIDS: looking ahead Nat Med 9, 887-91, 2003

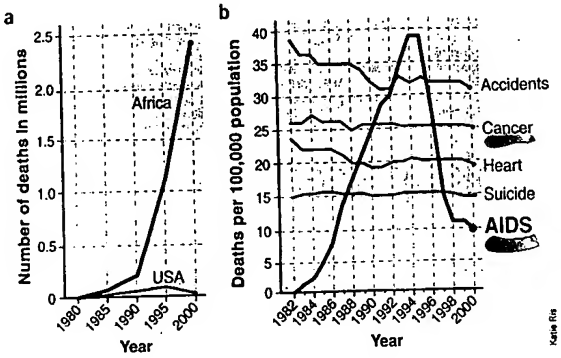

Figure 1 The human toll of AIDS. (a) Comparison of annual deaths from AIDS between sub-Saharan Africa (population 640 million) and the United States (population 273 million). (b) The five leading causes of death in men and women aged 25–44 years in the United States. Over the course of 10 years, AIDS came to be the chief cause of death in this generally healthy age group. The precipitous fall in mortality followed the introduction of highly active antiretroviral therapy (HAART), although the prevalence of HIV infection has not decreased. Reproduced with permission from ref. 58 from data provided by the Joint United Nations Programme on HIV/AIDS and the US Centers for Disease Control and Prevention.

Epidemiological evidence for the transmission of HIV by sexual and parenteral routes was clear before HIV was identified, and mother-to-child transmission soon after. The modes of transmission remain the same today and seem unlikely to change tomorrow. I previously questioned[1] whether biting insects with large mouthparts might act as 'dirty needles' to transfer HIV passively, given that another lentivirus—equine infectious anemia virus—is transmitted in this way. But there is no evidence of transmission by insects, and if it were occurring then we would expect to see more children seroconverting before puberty.

It was recently postulated[15] that in Africa, contaminated syringes and needles are responsible for more HIV transmission than is sexual contact. Although the number of infections by unsterile injections may have been underestimated during the pandemic phase of HIV, as well as during the mid-twentieth century[16], sexual spread is driving the African pandemic[17,18]. If injection were the main route of HIV infection in Africa, as it has been in eastern Europe and China, then again we would expect to see more children of HIV-negative parents developing AIDS.

As Valdiserri *et al.*[19] argue in this issue, much has been accomplished in reducing the transmission of HIV and, given political will, persuasive 'risk' education and sufficient resources, "the science exists to turn the pandemic around." Certainly, the continuing spread of disease could be slowed significantly, as has been seen in Senegal, Thailand and Uganda, but whether without an efficacious vaccine we can reduce R_0 to less than one—that is, reduce the mean rate of transmission from one infected person to less than one other person—remains speculative. India is currently estimated to have 4 million people infected with HIV (second only to South Africa), and this number could rise to 24 million in the next 10 years.

Perhaps we should not be too pessimistic. People do change their outlook and lifestyle in the face of devastating disease. For example, male circumcision has been identified as a factor that lessens the risk of female-to-male HIV infection in Africa[20]. Who would have thought a few years ago that men imbued with their traditional social customs would readily come forward to take part in randomized controlled trials of adult circumcision?[21]

Cell-to-cell transmission and tropism. Whereas the 'sexual synapse' is a frequent route of HIV transmission from one person to another—one that may be blocked specifically by a condom and hopefully one day by vaginal virucides—the 'immunological synapse' is a pathway for virus transmission from cell to cell (see accompanying review in this issue)[22] and has been elegantly shown[23] for human T-cell lymphotropic virus type I. We are only just beginning to understand the impact of the multiple delivery of virions from dendritic or other antigen-presenting cells to $CD4^+$ T-helper-cells.

I propose that the immunological synapse may account for the recent observation that although only a small proportion of $CD4^+$ T-cells in a lymphoid organ are infected by HIV, these cells contain several proviruses[24]. This type of 'multihit' infection at the cellular level may overcome the saturatable restriction factors of the host cell[25,26]. Packaged RNA genomes transcribed from more than one provirus in the same infected cell will assemble into heterozygous virions, which in turn will accelerate genetic recombination[24] and the evolution of drug resistance and immune escape.

In the future, we should pay more attention to the comparative pathology of lentiviruses, including HIV-2 (ref. 27). In this issue, Stevenson[11] points to the lessons to be learned from primates that are naturally infected with a high viral load but do not develop disease. He contrasts oncoviruses to HIV and the primate lentiviruses that can infect nondividing macrophages and dendritic cells. I argue further that all lentiviruses are macrophage-tropic, but only some infect lymphocytes (primate and feline immunodeficiency viruses). For example, let us consider Maedi-Visna virus, which is solely macrophage-tropic. Maedi-Visna in sheep is the prototypic disease from which lentiviruses derive their name[28]. Infected sheep develop a wasting disease and neurodegeneration similar to that seen in humans with AIDS, but they do not show T-helper-cell immune deficiency. As Maedi-Visna is remorselessly progressive, with a high rate of mortality, I have argued previously[29] that the infection, activation and apoptosis of T-cells in HIV are epiphenomena alongside the underlying progression of macrophage disease. Like the prophecies of Cassandra, this view remains unheeded perhaps because it would necessitate a complete reappraisal of both HIV pathogenesis and the inability of the immune system to ultimately control lentivirus infection.

Variation in HIV: evolution or noise? Such a question has been posed for the

[58] Weiss RA. HIV and AIDS: in relation to other pandemics. EMBO Rep 4, S10-S14 (2003)

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Molecular size and conformation of immunoglobulins.

Dorrington KJ, Tanford C.

molecular dimensions obtained from other measurements, when interpreted in terms of a rigid ellipsoid, a value near 220 nsec. would have been anticipated. Indeed, measurements of the rotational relaxation time for horse γG by dielectric dispersion (Oncley, 1943) and human γG by electric birefringence relaxation (Krause and O'Konski, 1965) have given values of 220 and 200 nsec., respectively. Electric birefringence studies on bovine γG gave rotational relaxation times of 215 nsec. (Ingram and Jerrard, 1963.) The discrepancies in the relaxation times provided by fluorescence depolarization measurements and other methods was interpreted to mean that different regions of the γG molecule could rotate independently; a situation which could be envisaged in the Noelken *et al.* model.

More recently this interpretation of the fluorescence depolarization data has been challenged (Weltman and Edelman, 1967; Wahl and Weber, 1967). These workers suggest that thermally activated rotations of the covalently bound DNS groups can occur independently of the rotation of the region of the molecule to which they are attached thus leading to low values for the rotational relaxation time of the protein. The use of fluorescence depolarization to determine molecular relaxation times depends on the requirement that the fluorescent label should be immobilized by strong interactions with the protein molecule. Weltman and Edelman (1967) and Wahl and Weber (1967) showed that the slopes of the fluorescence depolarization curves obtained isothermally at varying viscosities (sucrose isotherms) are smaller than the slopes obtained when the temperature is changed to alter the viscosity of the solvent without sucrose. Values of the rotational relaxation time calculated from sucrose isotherms at different temperatures ranged from 191 to 244 nsec., whereas heating curves gave values below 100 nsec. in agreement with earlier studies. These results seemed to indicate that under experimental conditions where free rotation of the dye molecules is minimized, values of the rotational relaxation time can be obtained from fluorescence studies which are apparently consistent with values obtained by other methods and previously calculated molecular dimensions. This does not appear to be the whole story according to a recent paper by Zagyansky *et al.* (1969). The latter have shown that dimethylaminonaphthalene sulfonyl chloride (DNS) conjugates of human and rabbit γG have different fluorescence properties from DNS conjugates of serum albumin and ovalbumin. Of particular relevance was the finding that the lifetime of the excited state for DNS γG was shorter (7.3 nsec.) than for DNS albumin (12.1 nsec.). Since the value of the lifetime of the excited state (τ) is required in the depolarization calculations, exact knowledge of it is of great importance. Zagyansky *et al.* (1969) calculated the rotational

Zagyansky, Y. A., Nezlin, R. S., and Tumerman, L. A. (1969). *Immunochemistry* 6, 787–800.

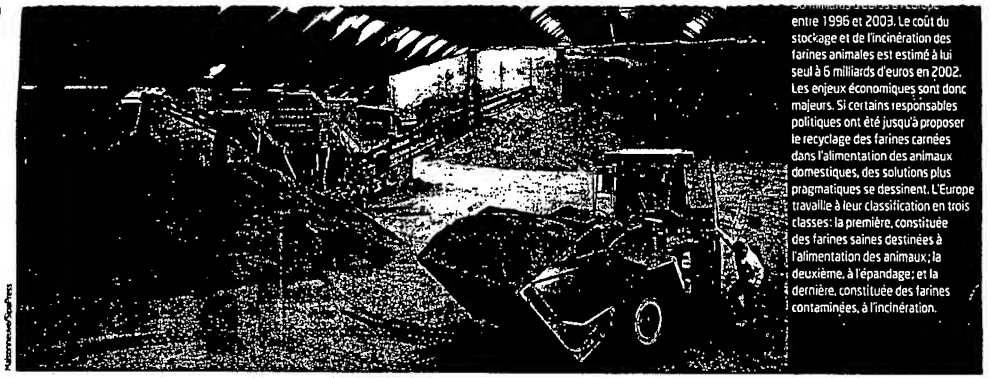
relaxation times of the DNS γG to be near 60 nsec. using sucrose isotherms and $\tau = 7.3$ nsec. Recalculation of the data of Weltman and Edelman (1967) and Wahl and Weber (1967) gives values of 100 to 130 nsec. using the lower lifetime value. The even lower value of 60 nsec. obtained by Zagyansky *et al.* may have been due, in part, to their removal of aggregates from the DNS γG preparations before the fluorescence measurements. These authors also provide some experimental evidence that the shorter lifetime of the excited state in DNS γG may be explained either by the substitution of DNS onto different amino acid side chains, the alternative conjugates having different spectral properties, or by differences in the hydrophobic nature of the environment of the DNS groups between DNS γG and DNS BSA. DNS–aspartate transaminase seems to have similar fluorescence lifetime properties to DNS γG (Polyanovksy *et al.*, 1970).

It seems from the above discussion that, even allowing for free rotation of the dye molecules, the rotational relaxation time for DNS γG is lower than expected for a rigid molecule. Thus it would seem that the units of the γG molecule with some rotational freedom are smaller than the whole molecule, and it is tempting to suggest that they correspond to the Fab and Fc fragments.

Two recent papers have reported fluorescence polarization measurements by direct measurement of the relaxation process (time span in the nanosecond range) following excitation by very short light pulses. This technique is free from some of the ambiguities that apply to previous results obtained by steady state measurements under constant illumination. Wahl (1969) employed DNS γG, with the DNS coupled covalently to the protein. His results were analyzed in terms of two relaxation processes, with relaxation times of 370 and 23 nsec. The first, which accounts for 65% of the overall relaxation process, is ascribed to rotation of the whole molecule and the second to internal Brownian movements of a globular region of the molecule. (The relaxation time, however, is much too short to represent a globular region of the size of the Fab region of the molecule.)

The second paper using the nanosecond fluorescence technique is by Yguerabide *et al.* (1970). They coupled the DNS chromophore to γG noncovalently by using γG that was an antibody directed against it. They also observed two relaxation times, one of 500 nsec., which is of the same order of magnitude as Wahl's longer relaxation time. The shorter relaxation time, however, was found to be 100 nsec., i.e., four times as large as Wahl's. When the same measurements were carried out with the complex between the DNS hapten and the Fab fragment of the antibody, only a single relaxation time of 100 nsec. was observed. The 100 nsec. relaxation

Polyanovsky, O. L., Zagyansky, Y. A., and Tumerman, L. A. (1970). *Mol. Biol. USSR.*



entre 1996 et 2003. Le coût du stockage et de l'incinération des farines animales est estimé à lui seul à 6 milliards d'euros en 2002. Les enjeux économiques sont donc majeurs. Si certains responsables politiques ont été jusqu'à proposer le recyclage des farines carnées dans l'alimentation des animaux domestiques, des solutions plus pragmatiques se dessinent. L'Europe travaille à leur classification en trois classes: la première, constituée des farines saines destinées à l'alimentation des animaux; la deuxième, à l'épandage; et la dernière, constituée des farines contaminées, à l'incinération.

Dix ans après la crise et alors que le nombre de cas d'ESB est en baisse, l'Europe envisage déjà de réintroduire les farines animales... pourtant à l'origine de l'épizootie. La Commission européenne programme leur retour d'ici à deux ans. L'Afssa exprime de fortes réserves.

„Impact Médecine" N°166 • 22 au 28 juin 2006

VACHE FOLLE

POLÉMIQUE SUR LE RETOUR DES FARINES ANIMALES

Mars 1996: l'Europe et le monde découvrent avec effroi que l'encéphalopathie spongiforme bovine (ESB) pourrait se transmettre à l'homme; dix cas atypiques de la maladie de Creutzfeldt-Jakob en Grande-Bretagne sont soupçonnés d'être liés à l'ESB. La psychose s'installe et les ventes de viande bovine s'effondrent.

Dix ans après cette crise alimentaire sans précédent, le danger semble écarté... et l'Europe parle déjà de réintroduire les farines animales. Pourtant, c'est bien elles qui sont incriminées. Depuis la sécurisation des farines de viande et d'os (FVO) en 1996 et leur interdiction totale en Europe au début de 2001, la prévalence de l'ESB a décliné. L'exemple français est éloquent. En 2001, 3,5 cas d'ESB ont été détectés pour 100 000 tests réalisés à l'abattoir, contre 0,5 cas en 2005.

Une ouverture progressive des verrous

Devant cette baisse et le succès des mesures adoptées, l'heure est incontestablement à l'assoupissement. Paradoxal? Peut-être. Quoi qu'il en soit, les faits abondent tous dans le même sens. L'exemple le plus récent est bien évidemment la réintroduction du boeuf britannique sur le marché européen décidée en mars dernier par la Commission de Bruxelles. Mais le glissement s'opère depuis déjà plus longtemps et de façon discrète. 5 août 2005: alors que l'Europe est en vacances, la Commission propose la réintroduction des farines de poisson, sous conditions, dans l'alimentation des animaux de ferme. Le 17 mai dernier, le Parlement se prononce favorablement sur cette proposition, notamment pour les jeunes ruminants séparés de leur mère. «Ce ne sera qu'une étape avant une réintroduction plus large des farines animales. L'échéance est estimée à environ deux ans», souligne Elke Anklam, chef du service de sécurité et de qualité alimentaire au sein de l'IRMM (Institut européen pour la recherche sur les matériaux de référence et de mesure).

N'y a-t-il donc aucun risque à réintroduire les farines animales? La polémique n'est pas close. «Des enjeux se télescopent avec des objectifs différents, relève le Dr Muriel Eliaszewicz, responsable de l'unité d'évaluation des risques biologiques à l'Agence française de sécurité sanitaire des aliments (Afssa). La Commission européenne n'a pas seulement en tête des considérations scientifiques et sanitaires. Elles sont aussi économiques.» En effet, la gestion des FVO coûte cher. L'ardoise s'élevait à 6 milliards d'euros environ en 2002, rien que pour leurs stockage et incinération. «La Commission discute de l'assouplissement des mesures de précaution sans avoir fait appel aux avis de l'Autorité de sécurité alimentaire européenne (Efsa)», s'inquiète le Dr Eliaszewicz, par ailleurs dubitative quant à l'intérêt scientifique de réintroduire les FVO (voir ci-dessous).

Du côté de la Commission européenne, on fait valoir l'intérêt diététique des FVO, tout en reconnaissant que «la logique commerciale veut que l'on produise plus pour des coûts moindres». Mais l'on se veut rassurant: «L'une des conditions de l'utilisation des farines comme denrées alimentaires est qu'elles proviennent de carcasses d'animaux destinés à la consommation humaine, explique Elke Anklam. Nous travaillons sur un

suite page 9

Dr MURIEL ELIASZEWICZ, responsable de l'unité d'évaluation des risques biologiques à l'Afssa

«Trop d'incertitudes scientifiques»

Dix ans après la crise, quel bilan faites-vous?

Les mesures de précaution mises en œuvre depuis plusieurs années ont permis de maîtriser l'épizootie. Mais qui dit maîtrise ne dit pas disparition. Il faut rester en vigilance active, notamment dans le cadre des échanges commerciaux avec les autres pays.

L'Afssa est-elle favorable à une réintroduction des farines animales?

Les farines animales sont à l'origine de la crise. Nous restons donc extrêmement prudents sur toute sollicitation de réintroduction des FVO, hormis les farines de poisson. Une décision de cette ampleur doit s'appuyer sur une expertise scientifique solide, ce qui semble pour le moment faire défaut au niveau européen. Pour ce qui est de la France, une réflexion est en cours au sein de l'Afssa. Mais il existe encore beaucoup d'incertitudes scientifiques. Il est notamment indispensable de faire un bilan des enseignements tirés de toute la période où les FVO ont été interdites dans toutes les espèces, afin de déterminer s'il existe un intérêt zootechnique à faire manger des FVO aux animaux d'élevage... Sur ce dossier, les enjeux économiques sont énormes, et il ne faudrait pas qu'ils prennent le pas sur les considérations sanitaires et scientifiques.

Quels sont les risques?

Il faut absolument éviter le recyclage intra-espèce des farines animales. Or, si la Commission européenne décidait de réintroduire les FVO chez certaines espèces comme les porcs et les volailles, il est évident que le risque de contamination croisée ne peut être exclu. D'autant que la France compte de nombreuses exploitations mixtes. Comment la Commission compte gérer la bonne mise en œuvre des mesures sur le terrain? Comment cela va-t-il être contrôlé? Je demande à voir.

Chronologie d'une crise

- 1986 : 1er cas d'ESB au Royaume-Uni
- 1988 : le Royaume-Uni interdit les farines de viande et d'os dans l'alimentation des ruminants
- 1989 : la France interdit l'importation de FVO britanniques
- 1990 : la France interdit les FVO dans l'alimentation des bovins
- 1991 : 1er cas d'ESB en France
- 1994 : la France interdit les FVO dans l'alimentation de tous les ruminants
- Mars 1996 : le Royaume-Uni annonce la possible transmission de la maladie à l'homme (nouveau variant de la maladie de Creutzfeldt-Jakob). Embargo européen sur la viande bovine britannique.
- Avril 1996 : en France, retrait de certains abats à risque (MRS) de la chaîne alimentaire
- 2000 : retrait en Europe des MRS. La France interdit l'utilisation de toutes les FVO dans l'alimentation de tous les animaux d'élevage
- 2001 : l'interdiction devient européenne. Mise en place en Europe du dépistage systématique de l'ESB
- Mars 2006 : levée de l'embargo sur la viande britannique
- Mai 2006 : avis favorable du Parlement européen pour la réintroduction des farines de poisson.

suite de la page 4

marqueur chimique permettant de tracer les matériaux contaminés afin d'être sûr qu'ils ne se retrouvent pas dans les farines alimentaires. Pour le moment, les ruminants ne sont pas concernés par cette réintroduction, et il n'y aura pas de recyclage intra-espèce.» Dans un premier temps, les FVO issues de produits bovins, ovins et caprins ne devraient donc être qu'au menu des porcs et des volailles.

Chiffres clés en France

- 980 cas d'ESB depuis 1991
- 17 cas liés au nouveau variant de la MCJ, dont plus de 50 % survenus après 2004.
- 770 000 tonnes de farines animales entreposées au 31 décembre 2003

Pas de risque zéro

Mais si le test de détection chez les bovins doit permettre en théorie d'écarter de la chaîne alimentaire tous les animaux réellement dangereux, il existe des cas sporadiques susceptibles de réalimenter la diffusion de l'agent infectieux. Dans certains pays, où le dispositif de sécurisation est moins rigoureux, il est probable que des animaux malades «passent au travers des mailles du filet», reconnaît-on à demi-mot à la Direction générale de l'alimentation. «Si ces animaux se retrouvent dans la chaîne alimentaire, il faut être vigilant sur le risque de contaminations croisées, à savoir les mélanges accidentels entre granulés pour bovins et farines animales destinées aux porcs et aux volailles», met en garde Jeanne Brugère-Picoux, professeur de pathologie du bétail à l'École vétérinaire nationale de Maisons-Alfort. Le dernier cas d'ESB détecté au Canada en avril dernier vient confirmer cette crainte. La machinerie agricole utilisée pour expédier et recevoir les ingrédients autorisés et prohibés s'est révélée être à l'origine de la contamination.

Par ailleurs, si la crise a permis de faire progresser les connaissances sur les maladies à prions, de nombreuses zones d'ombre demeurent, comme une éventuelle contamination des caprins et ovins par l'ESB (trois cas suspects signalés). «Il existe trop d'incertitudes pour prendre des mesures de gestion à la légère», conclut le Dr Eliaszewicz. Dans tous les cas, si une telle décision est prise en Europe, la France, en théorie, devra s'y plier.

JEAN-PIERRE BARRESI ET MARIE DORMOY

ELKE ANKLAM, chef du service de sécurité et de qualité alimentaire au sein de l'IRMM (Union européenne)

«Les outils d'analyse sont aujourd'hui plus performants, et nous avons les moyens de mieux contrôler les farines animales. Le risque de contamination est donc minime.»

vMCJ: trop de questions, peu de réponses

«Le nombre de cas liés au variant de la maladie de Creutzfeldt-Jakob (vMCJ), qui est la forme humaine de l'encéphalopathie spongiforme bovine (ESB), ne représente qu'une infime minorité des cas de MCJ recensés. En effet, 85 % des MCJ sont liées à la forme sporadique (environ 100 cas par an en France), 10 % à la forme génétique et 5 % à la forme iatrogène (traitement par l'hormone de croissance, surtout)», explique le Dr Jean-Philippe Brandel, chercheur à la cellule nationale de référence des maladies de Creutzfeldt-Jakob et à l'unité Inserm 708 «neuroépidémiologie». Jusqu'à présent, 161 personnes contaminées par le vMCJ ont été signalées en Grande-Bretagne, et 17 en France, ce qui fait de notre pays le deuxième plus infecté au monde. La forte exposition de la population française s'explique en grande partie par les importations massives de dérivés bovins en provenance de Grande-Bretagne entre 1980 et 1996. Si ces faits sont connus avec précision, les incertitudes restent pourtant nombreuses. D'une part, concernant la période d'incubation de la maladie: «On l'estime à environ 10-15 ans, ce qui signifie que tous les cas ne se sont pas encore déclarés. En Grande-Bretagne, le pic des cas de vMCJ se situe en 2000 avec une chute rassurante des cas signalés depuis. Pour la France, la situation est différente car l'exposition à l'agent bovin s'est faite plus tardivement. Plus de 50 % des cas enregistrés l'ont été depuis 2004», affirme le Dr Brandel. D'autre part, c'est le problème de la transfusion sanguine qui préoccupe les scientifiques. En effet, contrairement aux autres formes de la maladie, le vMCJ se transmet par transfusion, ce qui laisse entrevoir l'apparition de cas post-transfusionnels dans les années à venir. «Le risque ne peut être évalué avec certitude. Il est vrai que nous ne disposons toujours pas de test périphérique pour tester les poches de sang», déplore le Dr Brandel.

Dr CLAUDE BRONNER, président d'Espace Géné

Unions: la bat

Comme prévu, l'éclatement syndical chez les médecins libéraux complique fortement l'élection à la présidence dans chaque union. Le «deuxième tour» promet d'être fortement houleux dans de nombreuses régions où aucun syndicat n'est sorti réellement majoritaire des élections. Si la CSMF est en mesure de conserver la présidence de trois régions (Picardie, Poitou-Charentes et Lorraine), pour le reste, elle devra compter sur les appuis locaux du SML. Dans ce jeu des alliances, les consignes nationales du SML semblent claires. «Entendez-vous de manière privilégiée avec la CSMF si elle vous a respecté», exhorte le Dr Dinorino Cabrera, président du SML. Mais c'est sans compter sur les rapprochements, affinités, appétits personnels des acteurs locaux qui risquent de changer fortement la donne. L'Alsace, première URML

Xavier Bertrand reçoit l

Suite au scrutin des unions régionales marqué par un net repli des signataires de la convention et une forte poussée des opposants. Le ministre de la Santé a souhaité rencontrer les syndicats de médecins libéraux. C'est la CSMF, conventionniste, qui a ouvert le bal dès le 14 juin. Fidèle à lui même, le Dr Michel Chassang, président de la confédération a demandé au ministre de «mettre le turbo et d'en finir avec le harcèlement des caisses». Un message que le SML, l'autre syndicat signataire de

La répartition d'internat en

Annoncé pour le mois de mai, l'arrêté fixant la répartition par spécialités et par régions des postes d'internat n'est toujours pas paru au *Journal officiel*. Pour les 5 202 candidats qui ont déjà passé les épreuves classantes nationales, c'est l'incertitude totale, tant que le nombre de postes à la rentrée prochaine n'est toujours pas connu. Pour la médecine générale, l'enjeu de la répartition géogra-